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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/876,412	06/07/2001	Daniel M. Ammon JR.	P02872	7301

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EXAMINER
GAKH, YELENA G

ART UNIT	PAPER NUMBER
1743	2

DATE MAILED: 07/08/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/876,412	AMMON, DANIEL M.	
	Examiner	Art Unit	
	Yelena G. Gakh, Ph.D.	1743	

-- The MAILING DATE of this communication appears on th cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 June 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) *16-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15* is/are rejected.

7)☒ Claim(s) *1 and 13* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

   I. Claims 1-15, drawn to a method of quantitatively analyzing a sample, classified in class 436, subclass 173.

   II. Claims 16-21, drawn to a method for quantifying analytes that are differently present in two biological samples, classified in class 436, subclass 45.

   III. Claims 22-26, drawn to a method of quantitatively evaluating drug interactions, classified in class 351, subclass 160.

The inventions are distinct, each from the other because of the following reasons:

Inventions I, II and III are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the method of Group II recites the step of separation of the analytes by liquid chromatography, which is not applicable to the methods of Group I and III, and the method of Group III comprises in-vivo samples, which cannot be treated by methods of Groups I or II.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

2. During a telephone conversation with John E. Thomas on 07/03/03 a provisional election was made with traverse to prosecute the invention of Group I, claims 1-15. Affirmation of this election must be made by applicant in replying to this Office action. Claims 16-26 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Specification

3. The following guidelines illustrate the preferred layout for the specification of a utility application. These guidelines are suggested for the applicant's use.

Arrangement of the Specification

As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in upper case, without underlining or bold type, as a section heading. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

(a) TITLE OF THE INVENTION.
(b) CROSS-REFERENCE TO RELATED APPLICATIONS.
(c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.
(d) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC (See 37 CFR 1.52(e)(5) and MPEP 608.05. Computer program listings (37 CFR 1.96(c)), "Sequence Listings" (37 CFR 1.821(c)), and tables having more than 50 pages of text are permitted to be submitted on compact discs.) or
REFERENCE TO A "MICROFICHE APPENDIX" (See MPEP § 608.05(a). "Microfiche Appendices" were accepted by the Office until March 1, 2001.)
(e) BACKGROUND OF THE INVENTION.
(1) Field of the Invention.
(2) Description of Related Art including information disclosed under 37 CFR 1.97 and 1.98.
(f) BRIEF SUMMARY OF THE INVENTION.
(g) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).
(h) DETAILED DESCRIPTION OF THE INVENTION.
(i) CLAIM OR CLAIMS (commencing on a separate sheet).
(j) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).
(k) SEQUENCE LISTING (See MPEP § 2424 and 37 CFR 1.821-1.825. A "Sequence Listing" is required on paper if the application discloses a nucleotide or amino acid sequence as defined in 37 CFR 1.821(a) and if the required "Sequence Listing" is not submitted as an electronic document on compact disc).

The present arrangement of the specification makes it difficult to understand and does not disclose an essence of the invention and its novelty over the prior art in a clear and definite form. The rearrangement of the specification according to the US practice is highly recommended.

Claim Objections

4. Claims 1 and 13 are objected to, since they recite "comparing mass spectrometry of the sample analyte with the mass spectrometry of the internal standard", which is a technically incorrect expression. Mass spectrometry is a method; what actually is compared are the signal intensities in mass spectra, and therefore the expression should be rewritten as "comparing signal intensities of the sample analyte with the signal intensities of the internal standard in mass **spectra**".

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-7 and 12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the method employing equation recited in claim 8, does not reasonably provide enablement for any other method. There is no way for anyone of ordinary skill in the art to practice a method of quantitatively analyzing a sample analyte by MALDI using internal standard without applying calibration curves, if the equation recited in claim 8 is not known. The equation of claim 8 seems to be derived on the basis of a lengthy and tedious experimental work; it would have been a burden for any practitioner of the method to reproduce such experimental work in order to deduce the equation, which correlates MALDI parameters of the analyte and those of the standard with their concentrations via the ratio of their

molecular weights. Moreover, deducing such equation requires application of the calibration curves, which contradicts the claimed method.

No example for employing the method recited in claim 3 to analysis of DNA or RNA, which are notoriously known as worse analytes than proteins for MALDI analysis, is disclosed in the specification, and therefore the specification does not provide any basis for enablement of this embodiment.

Claims 8 and 9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the specific conditions of MALDI experiments, described on pages 25 and 26, does not reasonably provide enablement for any other conditions. In particular, only specific matrix and specific solvent system, which are very important factors for the correct results of MALDI experiments, are disclosed as enabling for the method recited in claims 8 and 9. Also, such factors as choosing the right internal standard, i.e. the one, which molecular weight differs less than 30 kD from that of the analyte and which ionizes on the same functional groups, are described as critical for applying the equation recited in claim 8, and therefore can be considered as limiting for the method disclosed.

Claims 10 and 11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the method employing equation of claim 10 with known constant C, does not reasonably provide enablement for the method, in which this constant is not known. Applying the method of claims 10 and 11 without preliminary determination of constant C to quantitative analysis of the analyte is equivalent to solving an equation with two unknowns. There is no one of ordinary skills in the art who can practice the method recited in claims 10 and 11, without knowing constant C upfront.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

6. Claims 1-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites in its preamble "a method of quantitatively analyzing a sample analyte", however, it does not recite any method step which can lead to this analysis, since it is not clear,

how comparing "mass spectrometry" of the analyte and internal standard can lead to its quantitative analysis.

In claim 2 it is not clear, how the concentrations of the analyte and standard can be compared, if the concentration of the analyte is presumably unknown, according to the title of the method?

The same question arises for claims 8 and 10: how the analyte and the standard can be compared according to the equations recited in the claims, if the concentration of the analyte is unknown? The claims should recite the step of determining the concentration of the analyte from these equations.

While in claim 11 the analyte and the internal standard are defined as ionizing on different functional groups, no step for determining the constant C is recited, which leads to the question, how the quantitative analysis can be performed on the basis of one equation with two unknowns?

In claims 13-15 it is not clear if MALDI analysis is performed from the surface of a biomaterial, and in this case, at which point the internal standard is added? Is it added directly to the biomaterial? If it is added directly to the biomaterial, which may be a solid contact lens, how is it mixed with the analyte? These steps are crucial for understanding and performing the method, and therefore should be recited in the claims.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. **Claim 13** is rejected under 35 U.S.C. 102(b) as being anticipated by Nelson et al. (Anal. Chem.).

Nelson teaches a quantitative determination of proteins, in particular cytochrome c, by MALDI-TOF analysis by normalizing cytochrome c intensity to myoglobin intensity.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

11. **Claims 1-4, 7 and 12** rejected under 35 U.S.C. 103(a) as being unpatentable over Nelson.

Nelson discloses several equations derived for the calibration plots, indicating that the linear coefficients of the equations are defined by the "detection efficiency of the individual protein components and the composition of the analytical fluid" (page 1411, left column).

It would have been obvious for anyone of ordinary skill in the art to experimentally determine coefficients of the equations disclosed by Nelson for other analytes, and perform the quantitative analysis of the analyte using the equations with proper coefficients, rather than the calibration curves.

12. **Claims 14-15** are rejected under 35 U.S.C. 103(a) as being unpatentable over Nelson in view of Kingshott et al. (Anal. Biochem.).

Nelson does not teach performing MALDI-TOF analysis for the analyte in or on contact lenses.

Kingshott teaches direct detection of proteins by MALDI-TOF on contact lenses.

It would have been obvious for anyone of ordinary skills in the art to apply Nelson's method to the analyte in or on contact lenses, because Kingshott discloses importance of

detecting proteins, which lead to biofouling of contact lenses, and straightforwardness of such analysis by MALDI-TOF.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yelena G. Gakh, Ph.D. whose telephone number is (703) 306-5906. The examiner can normally be reached on 9:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill A. Warden can be reached on (703) 308-4037. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9310 for regular communications and (703) 872-9311 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0661.

Yelena G. Gakh
July 3, 2003